REMARKS

Reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

By this Amendment, claims 22, 32 and 34 have been amended, such amendments being fully supported in the as-filed specification.

The claims presently pending before the Examiner are 22-26, 28, 29 and 31-34.

SUPPORT FOR AMENDMENTS

Claim 22 has been amended as follows:

"22. Subcutaneous implants

- a core (i) comprising at least one active principle dispersed in a polymeric matrix essentially consisting of PLGA obtained by extrusion, wherein said active principle is at most 55% mass/mass of the total weight of the core,

- a coating (ii) in film form comprising as the main component PLGA, **said PLGA having a molecular weight between 50,000 and 150,000 and a molar ratio of lactic acid to glycolic acid monomers between 50:50 and 95:5**,

- **having an extended overall active principle release with a linear profile".**

The first amendment finds support at paragraph 0109 of the published PCT application, whereas the second amendment finds antecedent support at paragraphs 0001, 0124, 0128, 0132, 0151, 0163, 0173 and in the working Examples.

Claims 32 and 34 have been amended by deleting the term "comprised" in order to overcome the objection raised under 32 USC § 112, as well as for consistency with the wording of all the other claims.

The Examiner has rejected claim 22 as being obvious over Chou et al. (US 2004/0009222) under 35 USC § 103(a). This rejection is traversed.

In order to overcome this objections Applicants have amended the independent product claim 22 by the provision that PLGA in the coating has a molecular weight between 50,000 and 150,000 and a molar ratio of lactic acid to

glycolic acid monomers between 50:50 and 95:5 and by expressly introducing the property of an extended overall active principle release with a linear profile of the claimed implants.

At page 4 of the outstanding Office Action, the Examiner reaffirms that, in view of Chou et al., "it would have been obvious to one of ordinary skill in the art to have PLGA simultaneously in both regions where the drug composed 40% of the core". Later on, at page 10, when commenting the Applicants' arguments, the Examiner further asserts that "Since Chou et al. teach both PLGA and PCL in the core and demonstrate a similar release profile when they are each uncoated, one of ordinary skill would have found it obvious to employ PLGA as core polymer with a PLGA skin and had a reasonable expectation that a reduction in initial burst and linear release would result."

Applicants strongly disagree with the Examiner's position and in support to the non-obviousness of the claimed invention hereby present the following arguments.

As already pointed out in Applicants previous response, the field of endeavor of Chou et al. is the reduction of the initial burst in the **sustained release** of drugs. In this regard, a number of polymers are listed as being suitable for achieving this object, as being supposedly usable in the core and the outer tube of a coextruded device. All of the hypothetical combinations are therefore considered by the Examiner to be equivalent in providing the presumed reduction of initial burst and the more rapid achievement of a close to zero order release profile. In the Examiner's view, this makes the listed polymers definitely interchangeable among each other both in the core and in the coating, and is deemed by the Examiner to give the same technical effect.

However, the Examiner's conclusion is **contradicted** by the teaching of Chou et al. itself. The examples, especially with reference to Fig. 2 and Fig. 3, show that PLGA and PCL do not provide a similar profile. In addition, Chou et al. in paragraph 0065 (the same paragraph as cited in the Office Action, pages 11-12), last sentence, indicate that different polymers lead to variations in release rate, as well as different physical properties for extrusion, thus differently affecting the resulting delivery device.

Furthermore, it should also be noted that, again in paragraph 0065, Chou et al. teach that the release rate of FA is proportional to the drug loading level in the matrix, which means that the higher the drug loading, the higher the release rate,

and so the shorter the overall release duration, according to the context of the sustained release devices.

Moreover, in the subsequent sentence, Chou et al. specify that "Compared to PLGA, EVA largely retarded the release of FA". This means that, not only do different polymers have different release profiles, but also that EVA should be effectively considered as a coating when a significant retardation of the drug release is desired.

The information summarized above was, indeed, the information available from Chou et al. to one of ordinary skill in the art at the time the claimed invention was made.

The Examiner, besides disregarding what Chou et al. actually disclose, seems to believe that the higher the reduction of the initial (burst) release, the longer the drug release, as more drug is left in the matrix. However, this is not the case with PLGA-based implants according to the claimed invention, and this was demonstrated by the experimental data in the Declaration of Mr. P. Mauriac submitted together with Applicants' Amendment of March 27, 2009.

As a matter of fact, when a drug/PLGA composition is placed in an aqueous environment, water diffuses into the matrix to form domains of aqueous drug solution. Water in contact with polyester chains of PLGA permits hydrolysis of the ester bonds to occur. This hydrolysis releases acidic residues which, if they remain in the close surroundings of the ester bonds, will result in the occurrence of a further hydrolysis, thus promoting a kind of autocatalysis.

Aqueous effluents released from the claimed implant comprise drug and acidic residues in solution. This outward flow is compensated for by an inward flow of "fresh" water and this results, globally, in a decrease in the concentration of local acidic residues.

Therefore, a relatively fast release of the drug will result in a relatively low local acidic residue concentration and, consequently, in a relatively low hydrolysis rate. Vice versa, **a slow release rate of the drug will result in a high hydrolysis rate and, consequently, in a fast polymeric matrix degradation.**

The overall release duration of the claimed PLGA-based implants depends on the time over which the polymeric matrix will fully degrade. A relatively low release rate, leading to an early matrix degradation, will result in a relatively short overall release duration.

The purpose of the experimental data given in the above referenced Declaration was to illustrate the above described relationship between the initial release rate and the overall release duration. Applicants wish to clarify that, in this regard, the tested compositions were uncoated implants. These compositions were based on the same PLGA matrix (defined by MW and ratio between glycolide and lactide moieties) and differed only in the concentration of the drug within the matrix.

This experiment was aimed at demonstrating how the initial diffusion rate (depending on the drug concentration) affects the later phases of the release from PLGA matrixes. The results are clearly in line with the above described principle, i.e. a low early release rate is actually followed by an early matrix degradation and a short overall release duration is then observed.

Even if the drug loading range (28 % to 35 % m/m) of the implants used in the experiment in the Declaration is not the same as the drug loading range given by Chou et al. (40 % to 75 % m/m) in the figures concerned, the resulting comparison can, however, help in highlighting and making clear what happens in a PLGA based matrix when the initial drug release is decreased. Since Chou et al. clearly indicates that "the release rate is proportional to the drug loading level in the matrix" (paragraph 0065), it follows that the effects of water flows inside the matrix follow an analogous trend for both ranges of drug loadings. The secondary effect of water flows on ester bonds hydrolysis rate is based on intrinsic chemical properties of ester bonds, said effect also following the trend for both the drug loading ranges.

Now, once a matrix is coated with a skin, the resulting coating leads to a decrease of the overall concentration of the drug in the implant and an additional distance to be covered by the drug before leaving the implant itself. Both these parameters act to decrease the diffusion rate and the water flows within the matrix, which confirms the experimental findings described in the subject application.

Actually, these findings provide evidence that PLGA-based implants should not be considered as "reservoir" type devices (e.g. based on inert matrix), as taught by Chou et al. (see e.g. par. 0005, 0002, 0025) and that **a reduction of initial release rate does not lead to a longer release duration.**

All of the Examples provided in this application, especially Example 3 and Figure 3B, strongly support the fact that the initial burst is strongly decreased and a far longer release is obtained by the claimed implants with respect to the corresponding (i.e. containing the same loading of the same drug in the same PLGA matrix) uncoated implants.

However, these results are entirely unexpected when compared with respect to the coated delivery devices of Chou et al. In fact, in view of the profile taught by Chou et al. involving a low initial burst release followed by a close to zero order profile, one of ordinary skill in the art would have observed a shorter overall release duration of the coated matrix with respect to the uncoated one. Therefore, starting from the teaching of Chou et al., one of ordinary skill in the art seeking to obtain a longer overall duration would have been led to try different polymers in the matrix. Furthermore, one of ordinary skill in the art **wishing to achieve both a lower initial burst and a longer overall duration**, would have been led to coat the matrix by using different polymers, particularly EVA, according to paragraph 0065.

This means that at the time the claimed invention was made, one of ordinary skill in the art having knowledge of Chou et al. would have only searched and been led in the direction of matrixes having the best possible result in reducing the initial burst, i.e. PCL, and coating successfully in extending the overall release duration, i.e. EVA.

Therefore, one of ordinary skill in the art would have definitely and unambiguously been led away from the claimed invention. This is the reason underlying the Applicants' assertion that Chou et al., indeed, teach away from the claimed solution found by Applicants.

As a matter of fact, there was no motivation at all for Applicants to consider any of the following claimed features:

- no reason to try a matrix consisting essentially of PLGA, because the known initial burst is shown to be worse than that observed for PCL;

- no reason to use an active principle in an amount at most 55% mass/mass of the total weight of the core, because a low active principle concentration teaches by implication a low release rate, leading to an early matrix degradation, that will result in a shorter overall release duration; therefore, this would have been believed to be an unsuitable parameter,

- no reason to consider a coating comprising as the main component PLGA, because of the teaching that compared to PLGA, EVA largely retards the release of the active principle; and,

- no reason to even select a PLGA having a molecular weight between 50,000 and 150,000 and a molar ratio of lactic acid to glycolic acid monomers between 50:50 and 95:5, because no disclosure at all can be found in Chou et al. about this feature.

Applicants, besides all the above indications to the contrary, surprisingly found that the **subcutaneous implants according to amended Claim 22**, involving PLGA both in the core and in the coating, resulted in achieving a **number of totally unexpected technical effects**, as shown in the current application and in the previously presented Declaration, namely:

~ the active principle in the PLGA matrix is not negatively affected by the extrusion production process;

~ the resulting coated matrix shows a very reduced initial burst **and** a prolonged and linear active principle release profile;

~ the risk of an undesirable second burst is avoided.

Therefore, the claimed invention is **non-obvious** and distinguishes over Chou et al., since Chou et al. besides teaching away from the claimed invention in many respects, **provides neither a suggestion nor a motivation to search in the direction of the claimed invention, while conversely being led to modify the teaching of Chou et al. to include PCL in the matrix and EVA in the coating**. The rejection having been overcome for failure to establish a *prima facie* case of obviousness should be withdrawn.

Claims 22, 26, and 28-29 were also rejected over Chou et al. in view of Talton, Belenkaya et al., Byon et al., and Yoon. The rejection is traversed.

However, none of the secondary prior art documents provides useful technical information for overcoming the teachings away, and the defects and deficiencies of the primary reference to Chou et al.

In particular, **Talton** has only been cited by the Examiner because PLGA is used in the coating. However, Talton discloses an invention concerning a method of coating particulate materials for oral (col. 16, line 54), injectable (col. 17, line 54) and nasal administration (col. 19, line 34), wherein the claims are directed to a fluidized bed coating apparatus. Additionally, since the object of the Talton invention is the coating process and apparatus, the nature of the particle core is definitely disregarded in this document, thus leading one to believe that the choice of the coating material is independent of the core to be coated.

Therefore, since Talton clearly does not pertain to the field of endeavour of the claimed invention being totally non-analogous, one of ordinary skill in the art would never have even considered Talton's teaching when presented with the problem which Applicants have solved herein.

However, even if hypothetically considered, it should be noted that Talton, at the point of the description cited by the Examiner, only states:

> "In preferred embodiments an organic polymer is selected for laser ablation and deposition onto the surface of pharmaceutical compounds. Particularly preferred as coating materials are organic compounds such as PLA, PGA, PLGA, and related biodegradable polymers, and functionalized derivatives thereof.
>
> The materials applied as coatings may act to modify the release rate or cell uptake of an active compound in the particle core. Such **sustained-release coatings** generally will act through diffusion or dissolution modification mechanisms.
>
> The coatings may also act to improve the physical stability of the drug particle, so as to improve, for example, its resistance to chipping or cracking. A coating may also serve as a moisture barrier, improving shelf-life of an otherwise rapidly degrading drug. Because of the potential for dry coating pharmaceutical particulates, use of the present invention is especially advantageous for coating to improve shelf-life. Thus, the present invention is especially applicable for coating pharmaceutical formulations which are sensitive to moisture, or solvents (such as proteins), and are therefore difficult to coat. This invention solves that problem." [emphasis added]

Therefore, one of ordinary skill in the art would only know that the coating can play a role in modifying the release rate or cell uptake of an active compound in the particle core, but it does not teach the direction of the presumed modification.

The total absence of any specific teaching in this regard is further confirmed by the paragraph titled "E. Coating compositions" where a very long ***"laundry"*** list of possible materials is presented, as follows:

> E. Coating Compositions
>
> The target materials used for the coating include most solids currently used in the pharmaceutical and food industries, namely any material that can be effectively ablated by the energy source. These materials include, but are not limited to, biodegradable and biocompatible polymers, polysaccharides, and proteins. Suitable biodegradable polymers include polylactides, polyglycolides, polycaprolactones, polydioxanones, polycarbonates, polyhydroxybutyrates, polyalkylene oxalates, polyanhydrides, polyamides, polyesteramides, polyurethanes, polyacetates, polyketals, polyorthocarbonates, polyphosphazenes, polyhydroxyvalerates, polyalkylene succinates, poly(malic acid), poly (amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polyorthoesters, and combinations thereof, as well as other polylactic acid polymers and copolymers, polyorthoesters, and polycaprolactones, etc. Suitable biocompatible polymers include polyethyleneglycols, polyvinylpyrrolidone, and polyvinylalcohols, etc. Suitable polysaccharides include dextrans, cellulose, xantham, chitins and chitosans, etc. Suitable proteins include polylysines and other polyamines, collagen, albumin, etc. A number of materials particularly useful as coating materials are disclosed in U.S. Pat. No. 5,702,716.

thus preventing one of ordinary skill in the art from having any reason to select PLGA, and even more so PLGA having a molecular weight between 50,000 and 150,000 and a molar ratio of lactic acid to glycolic acid monomers between 50:50 and 95:5.

It should be also noted that Talton not only refers to different ways of administration, but also concerns **sustained-release** particles, as demonstrated by Figs. 10, 11, 17, and 18, where it is shown that the **overall release** of the drug particles coated with PLGA takes **at most a few hours.**

Thus, one of ordinary skill in the art, even if he had hypothetically taken Talton's teaching into consideration, would never have found in Talton any useful information to be used in combination with Chou, Belenkaya and Byon for achieving the technical results of the claimed invention.

Additionally, Claim 22 is also non-obvious over Chou et al. in view of Talton as well as the other references, because every element of the invention has not been disclosed nor even suggested by Talton and the other references in combination, and thus the defects and teaching deficiencies of the primary reference, Chou et al. are not remedied or ameliorated by the secondary references to Talton, Belenkaya and Byon.

As a matter of fact, Talton does not dwell upon the nature of the core, thus completely disregarding the possibility of identifying and utilizing PLGA in the core. Therefore, one of ordinary skill in the art wishing to achieve a very reduced initial burst and a prolonged and linear active principle release profile, by combining these two prior art documents, would only have a further confirmation that PLGA is not suitable.

Belenkaya et al. relate "to the field of biodegradable hydrophilic nonwoven absorbents and more particularly to microfiber biodegradable absorbents prepared by the electrohydrodynamic method from blends of synthetic biodegradable polyesters and poly (N-vinyl) lactams which can be used for a variety of applications including wounds and burns dressings, drug carriers and for cosmetic applications." (see par. 0002)

Applicants respectfully submit that it is hardly understandable why one of ordinary skill in the art would have even taken this reference into consideration, inasmuch as the technical fields are so far removed from each other and entirely non-analogous.

The Examiner cites, in the outstanding Office Action, paragraph [0009], which recites:

> **[0009]** Some embodiments of the invention provide dressings, implants, dermatological compatible compositions and drug carrier compositions which include totally biodegradable non-gel materials having water, blood and other biological liquids absorption ability and possessing biological active properties like haemostatic and wound healing acceleration abilities, which are irreversible, retain their contour and shape when wet, and do not exhibit any swelling.

and paragraph [0041], which recites:

> **[0041]** Poly (d,l-lactide-co-glycolide) (PLGA) was dissolved in ethyl acetate to make a 20% (w/w) solution with solution viscosity 1-2 poise (Solution A) or a 10% (w/w) solution with solution viscosity 0.5 poise (Solution B). Poly-(N-vinyl) pyrrolidone (PVP) was dissolved in ethanol making a 20% (w/w) solution and mixed with the PLGA solution in ethyl acetate at PVP/PLGA ratio of 20/80 (w/w) that was used for the electrohydrodynamic spinning.

It is abundantly clear that neither of above cited paragraphs, nor the patent as a whole, could in any manner have assisted one of ordinary skill in the art in

finding any useful information for remedying the defects and deficiencies of the primary reference to Chou et al. as well as the secondary reference to Talton.

Byun et al. relates to "coated stents for carrying biologically active agents to provide localized treatment at the implant site and methods of applying stent coatings. In particular, this invention relates to antithrombogenic and antirestenotic stents having a multi-layered coating, wherein the first or inner layer is formed from a polymer and one or more biologically active agents, and a second or outer layer is formed from an antithrombogenic heparinized polymer." (see col. 1, lines 16-27)

Again, it is hard to understand why the one of ordinary skill in the art would have taken this patent into consideration, being that the technical fields are so far removed from the claimed invention as well as from the other cited prior art documents.

The Examiner refers to claims 1 and 2 of Byon et al. that recite respectively:

> 1. An article of manufacture comprising:
> a stent body comprising a surface; and
> a coating comprising at least two layers disposed over at least a portion of the stent body, wherein the at least two layers comprise a first layer disposed over the surface of the stent body and a second layer disposed over the first layer, said first layer comprising a polymer film having a biologically active agent dispersed therein, and the second layer comprising an antithrombogenic heparinized polymer comprising a macromolecule, a hydrophobic material, and heparin bound together by covalent bonds, wherein the hydrophobic material has more than one reactive functional group and under 100 mg/ml water solubility after being combined with the macromolecule.
>
> 2. The article of manufacture of claim 1 wherein the polymer film is selected from polyurethanes, polyethylene terephthalate, PLLA-poly-glycolic acid (PGA) copolymer (PLGA), polycaprolactone, poly-(hydroxybutyrate/hydroxyvalerate) copolymer, poly(vinylpyrrolidone), polytetrafluoroethylene, poly(2-hydroxyethylmethacrylate), poly(etherurethane urea), silicones, acrylics, epoxides, polyesters, urethanes, parlenes, polyphosphazene polymers, fluoropolymers, polyamides, polyolefins, and mixtures thereof.

It is clear that neither of above cited claims, nor the patent as a whole, could, in any manner, assist one of ordinary skill in the art in finding any useful information for remedying the defects and deficiencies of the primary reference to Chou et al. as well as the secondary reference to Talton and to Belenkaya et al..

Therefore, Claim 22 distinguishes over Chou et al. in view of Talton and in further view of Belenkaya et al. and Byun et al. Since the rejection has been overcome for failure to establish a *prima facie* case of obviousness by a preponderance of the evidence, withdrawal of the rejection is solicited.

Claims 22, and 33-34 stand rejected over the Dorta et al. article for obviousness under 35 USC § 103(a). This rejection is traversed.

Dorta et al. relate to three stacked layers, wherein the two external discs or layers contain PLGA, which leaves uncoated the 15% of the internal disc containing a drug.

The Examiner asserts that "there are no claim limitations drawn to a particular portion of the core being covered by the coating layer". Therefore, Dorta's article is still deemed to be relevant by the Examiner in spite of the arguments given in Applicants' previous response.

Applicants strongly traverse this rejection, since indeed according to MPEP 2111, "Claims must be given their broadest reasonable interpretation consistent with the specification":

> The Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR 1.75(d)(1).

Consequently, since nowhere in the current application have Applicants taught, nor even implicitly suggested that the core could only be partially coated, the assertion of the Examiner is respectfully rejected.

As a matter of fact, "the broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach (*In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999)). Thus, one of ordinary skill in the art would have never had any reason to

believe that the core of the claimed subcutaneous implants has some portion uncoated.

The foregoing provides the basis for why, in Applicants' previous response, the Dorta et al. article was deemed not to be relevant prior art.

However, even if hypothetically considered, it should be noted that **the implants of Dorta et al. are definitely not suitable in the context of the field of endeavour of the claimed invention.**

With reference to Fig. 5 of Dorta et al., the release profiles are reported of three stacked layers, wherein the external discs comprise PLGA having MW 47,000 and the internal disc has a drug content of 3% and 9%, respectively.

The concentration has been increased from 3% to 9% in order to avoid an undesirable initial lag-time, but in both instances the overall drug release occurred over not more than 20 days. Therefore, it is far removed from what one of ordinary skill in the art would consider when a much reduced initial burst and a prolonged and linear active principle release profile were sought to be achieved.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness. The § 103(a) rejection over Dorta has been overcome and should be withdrawn.

Claims 22-24 stand rejected under § 103(a) over Maquin et al. in view of Chou et al. This rejection is traversed.

The Examiner asserts that the arguments previously submitted are not limitations readable on the claims, particularly the drug release profile.

Applicants again traverse this position, since **both the reduced initial burst and the prolonged and linear drug release profile are technical effects deriving from the claimed selection and combination of the implant features.**

As a matter of fact, Claim 22 as previously presented involved all the essential features for achieving the object of the invention, i.e. for solving the technical problem underlying the invention, that is to obtain an implant which complies with all the requirements listed at paragraphs 0036-0040 of the as-filed specification, thus including a reduced initial burst and a prolonged and linear drug release profile.

Therefore, Applicants, in their previous response, argued the non-obviousness of the claimed implants defined by their essential features, by

comparing the unexpected and surprising technical results attained when compared with respect to the implants disclosed in Maquin et al.

Even though Applicants are of the opinion that the previously presented claim 22 was already in a distinct and exhaustive form so as to define the invention, in order to expedite the allowance of the application, these technical results are now recited in amended Claim 22.

Maquin et al. disclose compositions comprising a peptide and polylacticglycolic acid.

As mentioned previously with reference to the previously submitted Declaration, these types of compositions show a **tri-phase release pattern** were not only a first burst but also an earlier and bigger second burst can be observed, especially when the drug loading is reduced. This is evidenced also by Figures 3 and 4 of Maquin et al.

Therefore, one of ordinary skill in the art would have never even taken the teaching of Maquin into consideration, when seeking to achieve both a reduced initial burst **and** a prolonged and linear drug release profile, because the implants disclosed by Maquin are most definitely, unsuitable in the context of the claimed invention.

Furthermore, even if considered and combined with Chou et al., **one of ordinary skill in the art would have been led to believe that PLGA in the implants, according to Maquin et al., could have been successfully substituted with PCL and then coated with EVA, as taught by Chou et al., thus departing even further from the claimed invention.**

Thus, since the claimed invention distinguishes over the combination of Maquin and Chou, the § 103(a) rejection has been overcome and its withdrawal is solicited.

The Examiner has also maintained the rejection of Claims 22-25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 and 9 of **US Patent 6,620,422** (Maquin et al.) in view of Chou et al. This rejection is traversed.

As has been extensively demonstrated previously herein, currently amended claim 22 is patentable over the combination of Maquin et al. and Chou et al. This is further supported by the fact that **no feature of amended claim 22 overlaps the compositions of claim 1 of Maquin '422**. As a matter of fact, Maquin's

compositions only comprise a peptide having a particle size of 1 to 60 μm dispersed in a PLGA matrix, having a drug release profile in water, according to Claim 2, in three different stages, as referenced above.

Therefore, amended claim 22 does not overlap the scope of the cited claims of US Patent 6,620,422, since the coating is not present and the drug release profile is not linear.

Furthermore, the claimed implants also do not overlap the cited claims of US Patent 6,620,422 in view of Chou et al., because, as demonstrated above, one of ordinary skill in the art would have been led to believe that PLGA in the implants according to Maquin et al. would have been better substituted by PCL and then coated with EVA, as taught by Chou et al., thus **further departing from the claimed invention**, where both a reduced initial burst **and** a prolonged and linear drug release profile are achieved.

The double-patenting (non-statutory) rejection has been overcome and its withdrawal is solicited.

Applicants respectfully submit that having overcome all of the rejections of record, the issuance of a Notice of Allowance is in order and is solicited.

Please charge any fees which may be due and which have not been submitted herewith to our Deposit Account No. 01-0035.

Respectfully submitted,

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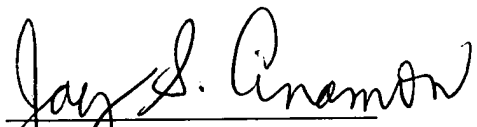
By 

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